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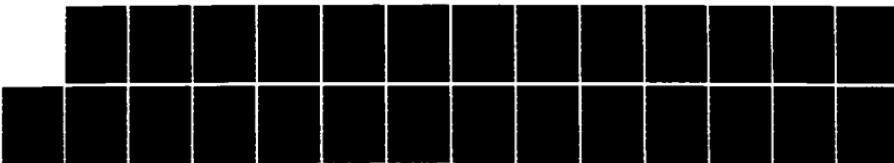
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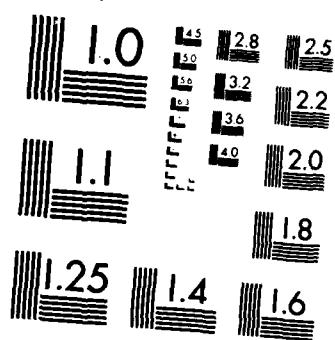
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and esophageal temperature ( $T_{es}$ ) were measured twice each min. Evaporative heat loss was calculated from changes in body weight. The displacement by heat storage of a theoretical temperature which is determined by heat exchange due to exercise and drug treatment, was calculated. A rational effective temperature ( $ET^*$ ) was derived using a psychrometric format and was used to assess the relative thermoregulatory strain for each treatment. ATR and 2-PAM treatment resulted in greater heat storage than SAL. Heat storage, when calculated from  $T_{re}$  was greater with CMB than with either drug alone. The  $ET^*$  was approximately  $2^{\circ}\text{C}$  higher with ATR or 2-PAM than with SAL, while CMB resulted in an increase of  $4.1^{\circ}\text{C}$  in  $ET^*$  above SAL. When heat storage was calculated from changes in  $T_{es}$  rather than  $T_{re}$ , the  $ET^*$  was increased by approximately  $4^{\circ}\text{C}$ , but was not as prominent as  $T_{re}$  in demonstrating differences between drugs. These data indicate that antidotal treatment (atropine and pralidoxime) for organophosphate poisoning will result in a significantly increased thermoregulatory strain than with either drug alone.

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**Exercise after atropine and pralidoxime increases the  
rational effective temperature**

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**Running head: Effective temperature after atropine and pralidoxime**

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## ABSTRACT

The purpose of the study was to determine the effect of antidotal treatment for organophosphate poisoning on heat exchange in four men during exercise at 55% peak aerobic power in a warm environment ( $T_a = 30.2 \pm 0.5^\circ\text{C}$ ;  $T_g = 30.3 \pm 0.5^\circ\text{C}$ ;  $P_w = 0.97 \pm 0.08 \text{ kPa}$ ). Each subject performed four experiments with the control treatment being an intramuscular (i.m.) injection of saline (SAL) which was compared to atropine (ATR; 2mg i.m.), pralidoxime (2-PAM; 600 mg i.m.) and atropine plus pralidoxime (CMB) treatment. Partitional calorimetric analysis was done at 25 min of exercise. Mean skin temperature, rectal temperature ( $T_{re}$ ) and esophageal temperature ( $T_{es}$ ) were measured twice each min. Evaporative heat loss was calculated from changes in body weight. The displacement by heat storage of a theoretical temperature, which is determined by heat exchange due to exercise and drug treatment, was calculated. A rational effective temperature ( $ET^*$ ) was derived using a psychrometric format and was used to assess the relative thermoregulatory strain for each treatment. ATR and 2-PAM treatment resulted in greater heat storage than SAL. Heat storage, when calculated from  $T_{re}$  was greater with CMB than with either drug alone. The  $ET^*$  was approximately  $2^\circ\text{C}$  higher with ATR or 2-PAM than with SAL, while CMB resulted in an increase of  $4.1^\circ\text{C}$  in  $ET^*$  above SAL. When heat storage was calculated from changes in  $T_{es}$  rather than  $T_{re}$ , the  $ET^*$  was increased by approximately  $4^\circ\text{C}$ , but was not as prominent as  $T_{re}$  in demonstrating differences between drugs. These data indicate that antidotal treatment (atropine and pralidoxime) for organophosphate poisoning will result in a significantly increased thermoregulatory strain than with either drug alone.

**Index terms:** Heat exchange, organophosphate poisoning antidote

A method has been developed which predicts equivalent environments that is based on the heat balance equation and defined in environmental terms (15). This rational or "new" effective temperature (ET\*) which was described is an imaginary temperature of an isothermal enclosure in which humans exchange the same total heat by radiation, convection and evaporation at the same skin wettedness (w) as observed in the actual environment. Nishi et al., (15) also reported that ET\* is an adequate index of thermal comfort and Gonzalez et al., (5) have confirmed the use of ET\* as an indicator of physiological strain for wide heat stress zones when the ambient water vapor pressure ( $P_w$ ) is greater than 2.67 kPa.

The ET\* has also been used to assess the thermoregulatory strain of exercise in a hot environment after atropine treatment (9). In those experiments, the inhibitory effect of atropine on sweating affected heat balance and thereby increased the ET\* from 41.5° to 45.5°C in unacclimated men. It has also been reported (10) that the ET\* is increased with atropine treatment in a warm, humid environment, although much less than in a hot environment, even though the wet bulb globe temperature (WBGT) index was similar in the two environments. Such studies indicate that the ET\* can be used successfully to assess the thermoregulatory effect of a provocative treatment with drugs which are known to inhibit the thermoregulatory effectors during exercise in a comfortable environment.

The purpose of the present investigation was to determine how the antidotal treatment, used in organophosphate poisoning, affected the ET\* of men exercising in a moderate environment. Although atropine treatment increased the ET\* of men exercising in two different environments (10), the effect of treatment with pralidoxime (2-PAM), a cholinesterase reactivator, and

the combination of 2-PAM and atropine on ET\*, as an index of heat exchange, is not known.

#### METHODS

Four men volunteered to be subjects for this investigation which was approved by the U.S. Army Human Use Research Committee. The subjects had an average ( $\pm$ S.D.) age of  $21 \pm 2$  yr, weight of  $81.2 \pm 9.8$  kg, height of  $182 \pm 9.1$  cm, DuBois surface area of  $2.00 \pm 0.2$  m<sup>2</sup> and % body fat (hydrostatic weighing) of  $18.7 \pm 4.4$  %.

Subjects were familiarized with the experimental techniques and environment prior to testing, but were not heat acclimated. Peak aerobic power (VO<sub>2</sub> peak) was measured for each subject (12) and was used to determine the relative work intensity for each subject. The experiments were done during November in an environmental chamber which had an ambient temperature (T<sub>a</sub>) of  $30.2 (\pm 0.5)^{\circ}\text{C}$ , black globe temperature (T<sub>g</sub>) of  $30.3 (\pm 0.5)^{\circ}\text{C}$ , ambient water vapor pressure (P<sub>w</sub>) of  $0.95 (\pm 0.1)$  kPa, and wind velocity of approximately  $0.3 \text{ m}\cdot\text{s}^{-1}$ . The average convective heat transfer coefficient (h<sub>c</sub>) was calculated to be  $6.0 \text{ W}\cdot\text{m}^{-2}\cdot\text{K}^{-1}$  (14) and the radiative heat transfer coefficient was calculated for each experiment. The combined radiant and convective heat transfer coefficient (hF<sub>Cl</sub>) was calculated from the equation:

$$hF_{Cl} = (h_r + h_c)(1 + 0.155(h_r + h_c)I_{clo})^{-1} \quad \text{W}\cdot\text{m}^{-2}\cdot\text{K}^{-1}$$

where I<sub>clo</sub> is clothing insulation (15), in clo units ( $1 \text{ clo} = 0.155 \text{ m}^2\cdot\text{K}\cdot\text{W}^{-1}$ ) and assumed to be 0.05 clo in this study. (The men exercised while dressed in shorts, shoes and socks.) The maximal evaporative capacity (E<sub>max</sub>) of the environment (4) averaged  $408 \text{ W}\cdot\text{m}^{-2}$  for saline treatment,  $473 \text{ W}\cdot\text{m}^{-2}$  for atropine,  $406 \text{ W}\cdot\text{min}^{-2}$  for pralidoxime and  $477 \text{ W}\cdot\text{m}^{-2}$  for pralidoxime plus atropine. All experiments were done between 0700 and 1000 h and were standardized for time of day for each subject to avoid circadian differences in thermoregulation (18).

Subjects were tested on four separate days, with each experiment being at least 48 h apart. The first day of testing was after the intramuscular (i.m.) injection of 1 ml of sterile saline (SAL). The experimental protocol was then counterbalanced for drug treatment. For subsequent tests, 2 mg of atropine sulfate (ATR; Elkin-Sinn, Cherry Hill, NJ), 600 mg pralidoxime chloride (2-PAM; protopam chloride, Ayerst, NY, NY) or 2 mg atropine plus 600 mg pralidoxime chloride (CMB) was administered i.m..

The experiment included a 5 min control period after instrumentation and equilibration, the injection of the appropriate drug, 30 min rest, and 30 min of exercise at 55%  $\dot{V}O_2$  peak on a modified cycle ergometer (1). Esophageal temperature ( $T_{es}$ ), rectal temperature ( $T_{re}$ ) and an eight site mean weighted skin temperature ( $T_{sk}$ ) were measured continuously. Metabolic heat production ( $M$ ) was estimated at 15 min of rest, and 10 and 25 min of exercise. Heart rate (HR) was measured at 2.5 min intervals. Total body sweating rate ( $g \cdot min^{-1}$ ) was calculated from pre- and post-experiment body weight.

Heat balance was calculated at 25 min of exercise for all experiments using the equation:

$$S = M_{sk} - (\text{sensible heat loss, } R+C) - (\text{skin evaporation, } E_{sk}), \text{ W} \cdot \text{m}^{-2} \quad (1)$$

$$\text{or } S = M_{sk} - hF_{Cl}(\bar{T}_{sk} - T_o) - w_e F_{pcl}(P_{s,sk} - P_w) \quad (1')$$

where  $S$  is the rate of body heat storage ( $\text{W} \cdot \text{m}^{-2}$ );  $M_{sk}$  is the net heat flow determined from ( $M - \text{Work} - C_{res} - E_{res}$ ) with the latter two factors being dry heat loss and evaporative heat loss from the lungs (7);  $hF_{Cl}$  and  $w_e F_{pcl}$  are combined radiative and convective heat transfer coefficient that govern sensible heat exchange and the evaporative heat transfer coefficient involving insensible heat exchange (6) respectively;  $w$  is the equivalent fraction of the total body surface ( $A_D$ ) wet with sweat which was calculated from  $E_{sk}/E_{max}$ ;  $P_{s,sk}$  is the

saturation vapor pressure (kPa) at mean skin temperature ( $\bar{T}_{sk}$ ); and  $P_w$  is the ambient water vapor pressure (kPa) calculated from dew point temperature.

This study used the psychrometric format to graphically describe the rate of heat storage as has been done previously (5,9,10,15). Nishi *et al.* (15) rewrote equation 1 to incorporate the heat balance equation as a function of ambient water vapor pressure and dry bulb temperature gradients in which

$$P_w - P_{s,sk} = -(\psi \cdot w^{-1})(T_o - (T_{act} + \Delta T_{stor})), \text{ kPa} \quad (2)$$

where  $\psi$  is a constant which is the ratio of the sensible heat transfer coefficient to the insensible heat transfer coefficient ( $hF_{Cl}/h_e F_{pcl}$ ).  $T_o$  is the operative temperature (5) of the test chamber in which

$$T_o = (h_r \bar{T}_r + h_c T_a) (h_r + h_c)^{-1}, {}^\circ\text{C} \quad (3)$$

in which  $\bar{T}_r$  (mean radiant temperature) is calculated from  $T_g + 2.2 v (T_g - T_a)$ , where  $v$  is the air velocity ( $\text{m} \cdot \text{s}^{-1}$ ).

The temperature ( $T_{act}$ ) in eq. 2 assumes that each of the subjects is in thermal balance regulated by sensible heat loss.

$$T_{act} = \bar{T}_{sk} - (M_{sk} \cdot hF_{Cl})^{-1}, {}^\circ\text{C} \quad (4)$$

Any displacement in heat storage ( $\Delta T_{stor}$ ) during a given exercise transient may be calculated as:

$$\Delta T_{stor} = ((\Delta \bar{T}_b \cdot \Delta t^{-1}) \cdot 0.97 (m_b \cdot A_D^{-1})) hF_{Cl}^{-1}, {}^\circ\text{C} \quad (5)$$

where  $(\Delta \bar{T}_b \cdot \Delta t^{-1})$  is the change in mean body temperature per h ( $\Delta T_{stor}$  was calculated from  $\Delta \bar{T}_b$  from the equation  $\bar{T}_b = 0.1 \bar{T}_{sk} + 0.9 T_c$  using both  $T_{re}$  and  $T_{es}$  as an index of core temperature ( $T_c$ )); 0.97 is the specific heat content of the tissues ( $\text{W} \cdot \text{h}^{-1} \cdot \text{kg}^{-1} \cdot \text{K}^{-1}$ );  $m_b$  is the lean body mass (kg);  $A_D$  is the DuBois surface area ( $\text{m}^2$ ) and  $hF_{Cl}$  is the combined heat transfer coefficient ( $\text{W} \cdot \text{m}^{-2} \cdot \text{K}^{-1}$ ).

Eq. 2 is represented on a psychrometric chart by a series of lines passing through a common point ( $CP = T_{act}, P_{s,sk}$ ). Any internal body heating caused by

exercise and drug treatment displaces the CP ( $T_{act} + T_{stor}$ ,  $P_{s,sk}$ ). The locus of any environmental condition (OP) is designated ( $T_0$ ,  $P_w$ ). If the CP and OP are connected (slope =  $-(\psi w^{-1})$ ), the point where this line crosses the 50% relative humidity curve on a psychrometric chart is the rational effective temperature (ET\*), defined by  $T_0$  on the X axis (15).

A one way analysis of variance was used to compare the heat exchange and ET\* data at the 25th min of exercise. Regression equations of both core temperature measurements over time were used to calculate the rate of change of heat content. Tukey's test of critical difference was used when needed. All differences are reported at  $P < 0.05$ .

## RESULTS

The drug treatments affected heat exchange during exercise with core temperature being significantly increased with ATR and CMB than with SAL or 2-PAM (Tables 1 and 2). All parameters of the heat balance equation were measured or calculated from measurements made at the 25th min of exercise. At that time, the subjects were in a thermoregulatory steady state when treated with saline. This was not true for all treatments.  $T_{es}$  increased more with ATR ( $1.2^\circ\text{C}$ ) and CMB ( $1.4^\circ\text{C}$ ) treatment than with saline treatment ( $0.7^\circ\text{C}$ ), although the  $T_{es}$  was not different with 2-PAM treatment ( $0.7^\circ\text{C}$ ).  $\bar{T}_{sk}$  increased more during ATR and CMB than in SAL and 2-PAM (Tables 1 and 2). The increase in core and skin temperatures observed with ATR and CMB can be explained by the decreased skin evaporative heat loss ( $E_{sk}$ ) due to inhibition of sweating (Table 3). Radiative and convective heat loss (R+C) were augmented in both ATR and CMB. Skin evaporative heat loss was also less with 2-PAM than SAL (Table 3), but R+C was only slightly greater than control.

In this investigation, core temperature was measured in the rectum and in the esophagus.  $\bar{T}_b$  and  $\Delta T_{stor}$  were also calculated using both indices of core temperature (Table 4).  $\Delta T_{stor}$  was greater when  $T_{es}$  was used as the index of core temperature than when  $T_{re}$  was used (Table 4). When calculated from  $T_{re}$ ,  $\Delta T_{stor}$  during CMB, averaged  $3.0^{\circ}\text{C}$  and  $1.9^{\circ}\text{C}$  greater than SAL and ATR respectively. 2-PAM did not significantly change  $\Delta T_{stor}$  from any other treatment. By using the psychrometric format to calculate  $ET^*$  from the heat balance equation and environmental conditions, the effect of the drugs on thermoregulation can be made clearer.  $ET^*$  was approximately  $2^{\circ}\text{C}$  greater during ATR and 2-PAM treatment than during SAL, while CMB resulted in an  $ET^*$   $4.1^{\circ}\text{C}$  greater than SAL.  $ET^*$  during CMB was also significantly greater than ATR or 2-PAM alone (Table 4, Fig. 1). The  $ET^*$  reflected the increase in  $\Delta T_{stor}$  when  $T_{es}$  was used as the core temperature index and was approximately  $4.0^{\circ}\text{C}$  higher than when calculated from  $T_{re}$ , but the interpretation of the data was different.  $ET^*$  during CMB was significantly increased over SAL, but was not different from ATR or 2-PAM.  $ET^*$  was not statistically different when SAL, ATR or 2-PAM treatment were compared (Table 4, Fig. 2).

## DISCUSSION

The rational effective temperature ( $ET^*$ ) is derived from the heat balance equation and certain biophysical parameters of the environment.  $ET^*$  has been used successfully as an index of heat exchange in different environments (5) and with atropine treatment (9,10). The present study, was used to assess the thermoregulatory effect of 2-PAM and a combination of 2-PAM plus atropine treatment during exercise.

The ET\* analysis was done graphically rather than by iteration (5). The ET\* evident after atropine treatment increased 2.0°C above saline treatment in the present study (Table 4) which is consistent with previous experiments (9,10). The competitive inhibition of sweating which occurred with atropine decreased the observed skin evaporative heat loss, although there was a greater heat loss by radiation and convection (R+C) than during saline treatment (Table 3). However, the greater R+C was not enough to compensate for the decreased skin evaporative heat loss, as has been shown previously (3,9,10), and  $T_{es}$  was significantly higher at the 25th min of exercise than present in the control (Table 2).

There have been many reports of cutaneous vasodilation occurring after atropine treatment related to the observation of the "mantle flush" (20) and to the report of Roddie *et al.* (17) of the acetylcholine-independent vasodilation in response to body heating. More recently, the calculated increase in radiative and convective heat loss during exercise after atropine described by Davies *et al.* (3) and Kolka *et al.* (9,10) clearly indicated atropine-induced vasodilation. These reports, together with the evidence that vasodilation can occur via a prostaglandin-mediated mechanism (13), lead us to postulate that the cutaneous vasodilation observed in this study is distinct from the acetylcholine-mediated vasodilation which requires an endothelium-derived releasing factor (8). We are aware that atropine does cross the blood-brain barrier (20) so the increased radiative and convective heat loss we observed might also be explained as a reflex vasodilation. That is, atropine may be acting to modify the hypothalamic signal for heat loss. One thermoregulatory effector, the sweat gland, is competitively inhibited at the Ach receptor by the drug, therefore, any amplification of effector outflow would be most prominent at the cutaneous vasculature. However, this interpretation would indicate that the

vasodilatory fibers to the cutaneous vasculature are not cholinergic (muscarinic) in nature.

2-PAM is used in organophosphate poisoning treatment as a reactivating agent for bound acetylcholinesterase (ChE) which allows the redevelopment of normal synaptic function (19). Treatment with 2-PAM also significantly affected heat exchange during exercise as indicated by the increased ET\* when compared with saline. The skin evaporative heat loss was less than and R+C was slightly, but not significantly, greater than saline treatment, although  $T_{es}$  was not significantly different from saline. The higher ET\* after 2-PAM treatment indicates that in a more extreme environment, heat exchange would be more seriously affected. The inhibitory effect of 2-PAM on sweating has been observed previously (2) during low intensity exercise, although 2-PAM did not affect core or skin temperature. It appears that moderately intense exercise is required (relatively high metabolic load) to exacerbate the effects of 2-PAM on heat exchange, as Robinson and McMichael, (16) and Cummings et al. (2) reported that 2-PAM did not affect core or skin temperature during rest and low intensity exercise.

A confirmation of our observation of sweating depression with 2-PAM, is the preliminary observation of the sweating rate in *e. patas* during passive heating at  $T_a$  of 30°C in which there occurred a depressed sweating rate (Elizondo, R.S., personal communication). This observation is of similar magnitude as that found in the present study (45%) when compared with saline treatment. Additionally, in one animal, the sweating suppression increased core temperature 0.2°C and skin conductance was increased. There was no core temperature increase with 2-PAM in a second animal, but there was an increased  $\bar{T}_{sk}$  (0.2°C) and increased skin conductance. The increased ET\*, and lower  $E_{sk}$

which was observed with 2-PAM in this study, is contradictory to reports of weak anti-ChE activity of the drug (19), which would indicate an augmented sweating rate because ChE inhibition would increase Ach available to the receptor. If organophosphate poisoning has not occurred, perhaps 2-PAM treatment activates otherwise inactive ChE, thus decreasing Ach available at the eccrine sweat gland receptor thereby decreasing sweating rate. Further studies are necessary to determine the exact mechanism of action on heat exchange with 2-PAM treatment.

During combined atropine and 2-PAM treatment, the ET\* was significantly increased above that observed with saline treatment and was higher than either atropine or 2-PAM alone. The observed skin evaporation was suppressed to the same degree as in ATR (Table 3) and R+C was significantly elevated above saline.  $\Delta T_{stor}$  was greater with CMB than with atropine alone (Table 4), and consequently, ET\* was significantly greater with CMB than ATR or 2-PAM alone. Therefore, the present study indicates a greater thermoregulatory strain with CMB than with atropine alone which is consistent with the data of Cummings *et al.* (2) and Robinson and McMichael (16). By analyzing the heat exchange data in the psychrometric format, the effect of CMB can be more clearly presented.

A secondary part of this study was to investigate whether the calculation of ET\* was affected by the index of core temperature measured. Both  $T_{re}$  and  $T_{es}$  were measured in the present study for two reasons. Previous studies of atropine effects on the rational effective temperature in this laboratory used  $T_{re}$  as an index of core temperature and we primarily wanted to be able to compare the data from the present study with those data (9,10). The experimental design of the present study was such that exercise continued for 30 min and metabolic rate was measured at the 25th min of exercise which was

enough time to overcome the lag in the  $T_{re}$  measurements. We therefore made our interpretation of the drug effects on ET\* from heat storage data calculated from  $T_{re}$ . Secondly, studies of dynamic temperature changes, such as those during short duration exercise, changing ambient water vapor pressure and thermal conditions, or cycles of work and rest, require a quickly responding index of core temperature and esophageal temperature is one of the most rapidly responding measures of core temperature (11). The major consequence of using  $T_{es}$  was a more rapid change in mean body temperature over time when compared to  $T_{re}$ , which is manifested in the larger  $\Delta T_{stor}$  calculated (Table 4) and greater displacement from the line connecting the CP and OP (Figs. 1 and 2). The resultant ET\* is thereby increased over that calculated from  $T_{re}$ . In this study, although the ET\* was much greater when calculated from  $T_{es}$  than  $T_{re}$ , the interpretation of the effect of the drugs was substantially different. The ET\* was only statistically different from SAL when the combination of ATR and 2-PAM was used. Furthermore, by calculating  $\Delta T_{stor}$  from  $T_{es}$  measurements, the derived effective temperature indicates a greater relative thermoregulatory strain than when  $\Delta T_{stor}$  is calculated from  $T_{re}$  (5,15).

In conclusion, the effect of treatment with atropine, pralidoxime or atropine plus pralidoxime on heat balance resulted in a significantly increased ET\*. Atropine and 2-PAM each increased ET\* by approximately 2.0°C while the combined drug treatment resulted in increasing ET\* by 4.2°C when  $T_{re}$  was used as an index of core temperature (Fig 1). 2-PAM treatment also indicated a thermoregulatory strain when heat exchange data are analyzed in the psychrometric format used in this study. Finally, the marked increase in ET\* during combined atropine and pralidoxime treatment indicated that the physiological strain was greater than when each drug was given separately.

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The opinions and/or findings contained in this report are those of the authors and should not be construed as official Department of the Army position, policy or decision unless so distinguished by other offical documentation.

Human subjects participated in these studies after giving their informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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**Table 1.** Mean ( $\pm$  S.D.)  $T_{es}$ ,  $T_{re}$ ,  $T_{sk}$ , HR, and M at rest during saline (SAL), atropine (ATR), pralidoxime (2-PAM) and ATR + 2-PAM (CMB) treatment.

	$T_{es}$ (°C)	$T_{re}$ (°C)	$T_{sk}$ (°C)	HR (beats·min <sup>-1</sup> )	M (W·m <sup>-2</sup> )
SAL	36.67 0.15	37.17 0.25	34.04 0.28	67 8	48.5 12.0
ATR	36.61 0.20	37.06 0.20	34.06 0.30	59 13	37.0 4.2
2-PAM	36.48 0.30	36.92 0.28	33.97 0.54	66 12	40.3 3.9
CMB	36.76 0.28	37.11 0.23	33.97 0.64	71 11	36.0 7.7

**Table 2.** Mean ( $\pm$  S.D.)  $T_{es}$ ,  $T_{re}$ ,  $T_{sk}$ , HR,  $P_{s,sk}$ ,  $E_{res}$ ,  $C_{res}$ , M and Work (W) at the 25th min of exercise during saline (SAL), atropine (ATR), pralidoxime (2-PAM) or ATR plus 2-PAM (CMB) treatment.

	$T_{es}$ (°C)	$T_{re}$ (°C)	$T_{sk}$ (°C)	HR (beats·min $^{-1}$ )	$P_{s,sk}$ (kPa)	$E_{res}$ (W·m $^{-2}$ )	$C_{res}$ (W·m $^{-2}$ )	M (W·m $^{-2}$ )	W (W·m $^{-2}$ )
SAL	37.37 0.15	37.64 0.15	33.62 0.51	130 5	5.21 0.1	30.1 3.6	2.02# 0.1	352.3 43.7	54.8 6.3
ATR	37.78* 0.18	37.62 0.15	35.79* 0.49	158* 4	5.88* 0.2	29.1 2.5	1.83 0.2	340.0 31.4	54.8 6.3
2-PAM	37.16+ 0.25	37.56 0.22	33.95+ 0.65	123 12	5.31+ 0.2	26.7* 3.0	1.70* 0.2	319.5 38.9	54.8 6.3
CMB	38.18*+# 0.27	37.81 0.30	36.40*+# 0.57	155* 2	6.07*+# 0.2	27.0* 2.0	1.50*+ 0.3	325.0 27.7	54.8 6.3

\*Different from saline ( $p < 0.05$ )

+Different from atropine ( $p < 0.05$ )

#Different from pralidoxime ( $p < 0.05$ )

**Table 3.** Mean ( $\pm$  S.D.)  $M_{sk}$ ,  $E_{sk}$ ,  $R+C$ ,  $w$  and  $T_{act}$  calculated from data collected at the 25th min of exercise and the environmental parameters  $T_o$  and  $P_a$  during saline (SAL), atropine (ATR), pralidoxime (2-PAM) or ATR plus 2-PAM (CMB) treatment.

	$M_{sk}$ ( $W \cdot m^{-2}$ )	$E_{sk}$ ( $W \cdot m^{-2}$ )	$R+C$ ( $W \cdot m^{-2}$ )	$w$	$T_{act}$ ( $^{\circ}C$ )	$T_o$ ( $^{\circ}C$ )	$P_a$ (kPa)
SAL	265.4 38.0	233.8 65.0	31.9 7.7	0.58 0.17	3.5 4.6	30.0 0.4	0.91 0.08
ATR	254.3 23.2	82.9* 33.1	49.7*# 6.5	0.18* 0.08	7.0 3.0	30.2 0.5	0.90 0.04
2-PAM	236.4 30.2	115.8* 50.5	34.2 6.7	0.29* 0.14	7.1 3.5	30.1 0.1	1.03 0.08
CMB	241.8 19.2	79.6* 55.0	49.8*# 2.8	0.17* 0.11	9.1* 2.3	30.8 0.4	1.05 0.09

\*Different from saline ( $p < 0.05$ )

+Different from atropine ( $p < 0.05$ )

#Different from pralidoxime ( $p < 0.05$ )

**Table 4.** Mean ( $\pm$  S.D.)  $\Delta T_{stor}$ , and ET\* calculated from  $T_{re}$  and  $\Delta T_{stor,Tes}$  and ET\* $Tes$  calculated from  $Tes$  and the OP and CP used in the psychrometric format.

	$\Delta T_{stor}$ (°C)	ET* (°C)	$\Delta T_{stor,Tes}$ (°C)	ET* $Tes$ (°C)	OP ( $T_o, P_w$ )	CP ( $T_{act}, P_s, sk$ )
SAL	6.0 1.3	29.0	12.9 3.0	33.3	30.0,0.91	3.5,5.21
ATR	7.1 1.7	31.0*	15.0 3.7	35.4	30.2,0.90	7.0,5.88
2-PAM	7.5 2.9	30.8*	15.8 2.3	35.3	30.1,1.03	7.1,5.31
CMB	9.0*+ 1.5	33.5*+#	14.2 4.2	36.3*	30.8,1.06	9.1,6.07

\*Different from saline ( $p < 0.05$ )

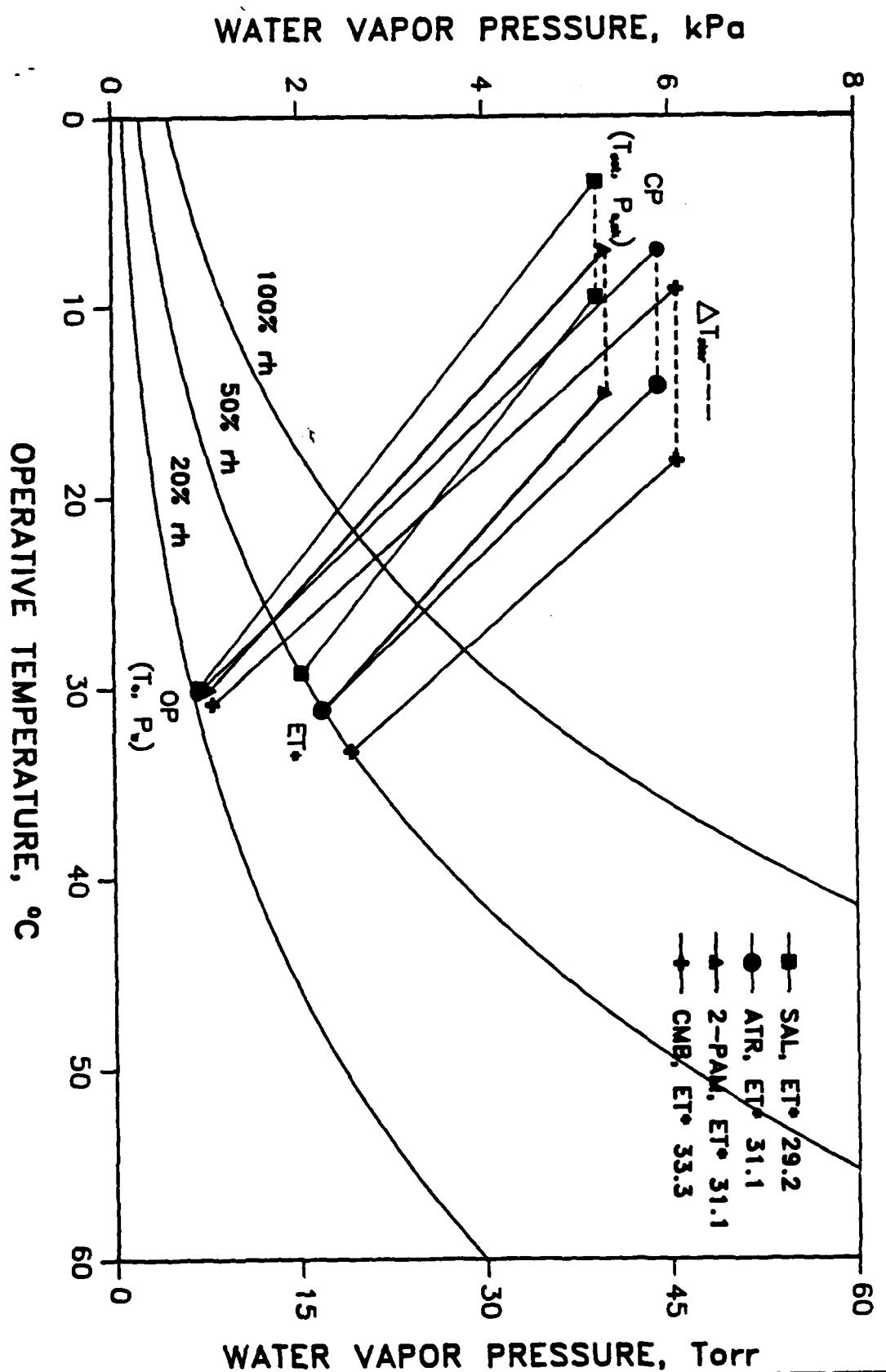
+Different from atropine ( $p < 0.05$ )

#Different from pralidoxime ( $p < 0.05$ )

### FIGURE LEGENDS

Figure 1. Graphic presentation of the mean rational effective temperature ( $ET^*$ ) resulting from internal body heating caused by exercise and the specific drug treatment which displaces the Common Point (CP) by  $\Delta T_{stor}$ . These data were calculated using  $T_{re}$  as core temperature.  $\Delta T_{stor}$  is heat storage;  $T_{act} = (T_{sk} - M_{sk}) (hFcl)^{-1}$ ;  $P_{s,sk}$  is saturation vapor pressure at the skin;  $T_o$  is operative temperatures;  $P_w$  is ambient water vapor pressure.

Figure 2. Graphic presentation of the mean rational effective temperature ( $ET^*$ ) resulting from internal body heating caused by exercise and the specific drug treatment which displaces the Common Point (CP) by  $\Delta T_{stor}$ . These data were calculated using  $T_{es}$  as core temperature.  $\Delta T_{stor}$  is heat storage;  $T_{act} = (T_{sk} - M_{sk}) (hFcl)^{-1}$ ;  $P_{s,sk}$  is saturation vapor pressure at the skin;  $t_o$  is operative temperature; and  $P_w$  is ambient water vapor pressure.



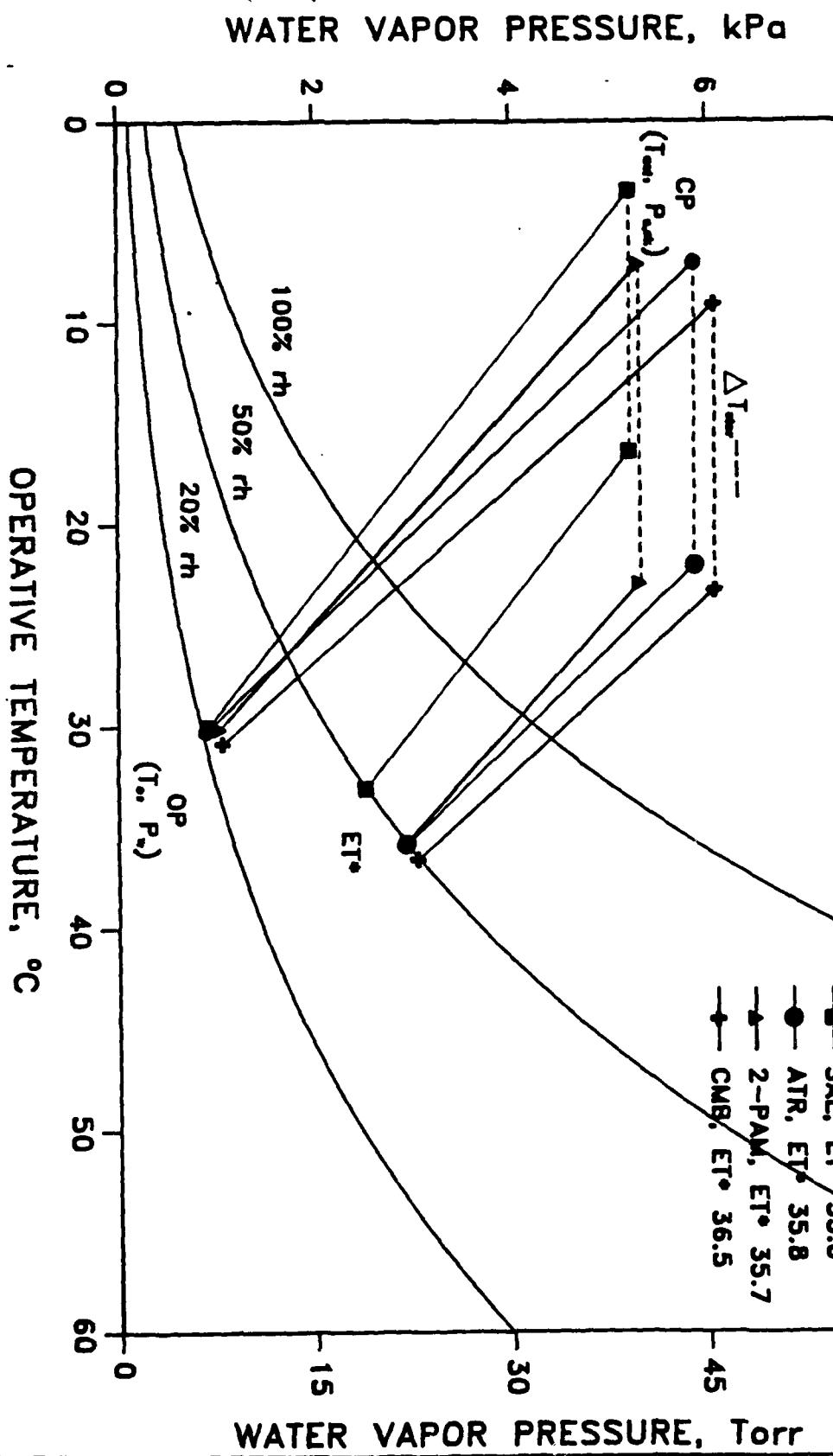
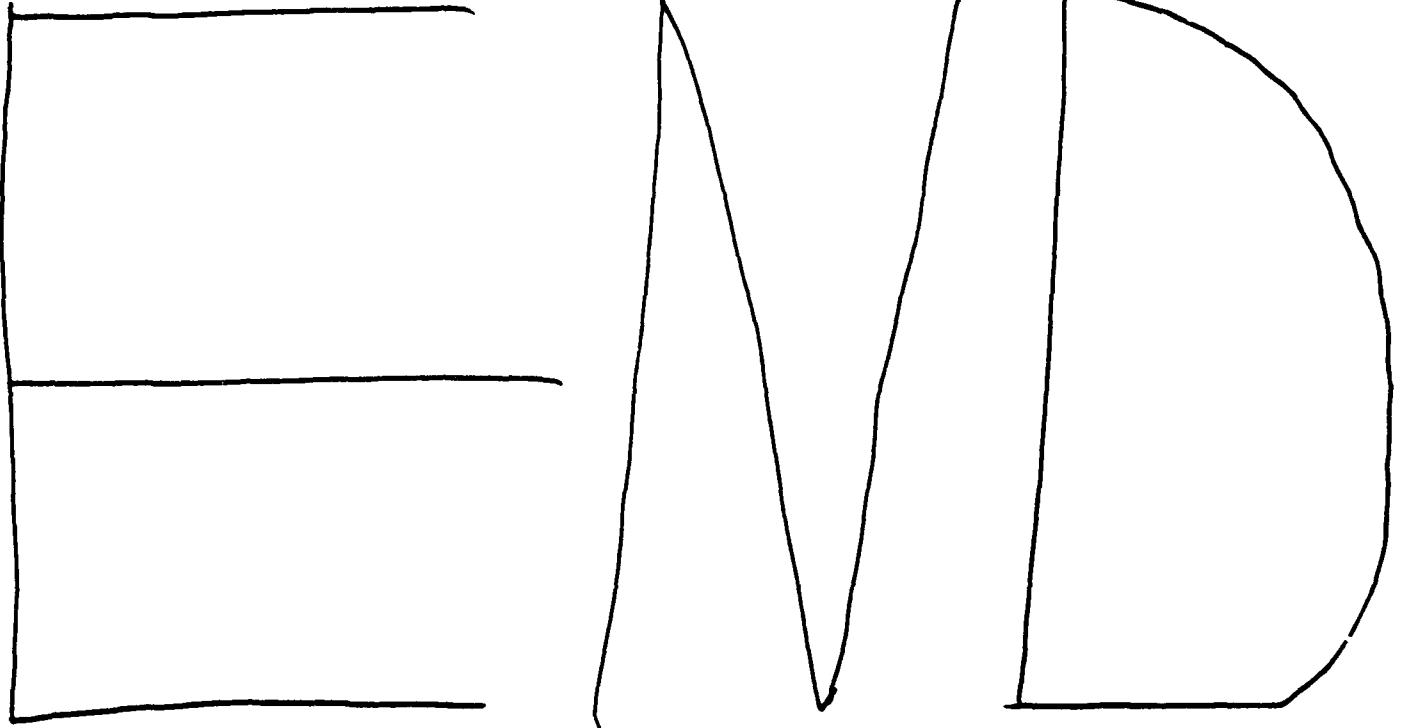


FIG. 2



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